correction. A simple Markov model was built to illustrate the impact of the half-cycle correction, and to demonstrate how a more accurate correction factor can be applied to models. **RESULTS:** Half-cycle corrections appear to be used routinely in Markov models. In nearly all cases, the so-called "correction" is applied without due consideration of the implications. Two major flaws were identified with the approach. The first, mathematical, flaw is that the half-cycle correction approach assumes that all events occur at the mid-point of each cycle. It can be demonstrated that, for one-directional events (such as death), events will be more likely to occur in the first half of the cycle since more patients will be exposed to the event at the start of the cycle, and the number of patients 'at risk' falls throughout the cycle. The second flaw is that, for many events, the implications of the event may not actually become apparent until the next cycle. For instance, in oncology, the increased costs associated with disease progression will not occur until progression is confirmed, which may only happen at regular routine follow-up visits. **CONCLUSIONS:** Half-cycle corrections are frequently applied inappropriately in modelling. This study has produced two key recommendations to generate more accurate outcomes and to avoid biases in decision analytic models.

PRM49

EQ-5D VERSUS DISEASE-SPECIFIC HR-QOL INSTRUMENTS – NO CONTEST?

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OBJECTIVES: To define the extent to which using the EQ-5D versus disease-specific instruments is critical in overall cost-effectiveness assessments, specifically regarding cost-utility. **METHODS:** Five ISPOR therapeutic areas (TAs) were randomly selected, and literature research found on PubMed for the UK, as well as other European publications, to retrieve publically available data on health state utility scores in the respective TAs. Data were extracted into a database and various model structures reconstructed in order to determine the impact of different HR-QoL instruments on overall cost-effectiveness. Standard Monte Carlo techniques were applied to generate simulations, informing both the expected cost-effectiveness and its associated uncertainty. Cost-utility as well as net monetary / health benefit were considered, based on willingness-to-pay for a QALY values ranging from zero to €100,000. Incremental cost-utility scatter-plots as well as cost-effectiveness acceptability curves were generated to illustrate how the results differ both deterministically and probabilistically. **RESULTS:** The mean percentage change in the cost-utility ratio across all five disease areas was app. 29% (a 95% confidence interval ranging from −21% to −42%). Similar but even stronger results were found when using incremental net monetary benefit measures. The therapeutic area with the most significant difference was oncology (36.5%), and the least significant was cardiovascular (19%). Other TAs were COPD, Parkinson's disease, and obesity. **CONCLUSIONS:** It was consistently found that cost-effectiveness results differed significantly when different HR-QoL measures were used. Since disease-specific instruments employ more sensitive criteria than generic ones, they generate more favourable cost-effectiveness results. Comparing the results of both generic and specific indicators in structural sensitivity analyses appears to be imperative to assess the consistency of value judgements derived from quantitative modelling.

PRM50

RANDOM NUMBER GENERATORS IN MONTE CARLO SIMULATION

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OBJECTIVES: Monte Carlo simulations are driven by the generation of pseudo random numbers (PRN). Testing the effectiveness of PRN generators is rarely undertaken yet any systematic pattern or bias has implications for simulation run time and accuracy. The objective of this study was to compare two commonly used PRN in an applied setting to illustrate potential implications of low performance. **METHODS:** The IMS Core Diabetes Model (CDM) was used to explore their precision in detecting the onset of end stage renal disease (ESRD using the MS-Visual C++ 2008 PRN generator (MSG) and Mersenne Twister generator (MTG). One-year probabilities of ESRD for a 65 year old female smoker were generated with a systolic blood pressure (SBP) of 135 mmHG (p=0.000363) and 140 mmHg (p=0.000444). The expected one-year incidence was compared to probabilistic observations in the CDM for both PRN generators. **RESULTS:** The expected yearly incidence of ESRD was 0.0363% (SBP 135 mmHg) and 0.0444% (SBP (140mmHG). Monte Carlo estimates were 0.0379% and 0.0477% using the MSG and 0.0239% for both SBP values using the MTG. The MSG overestimated expected rates by 4.41% and 7.4%; the MTG underestimated the probability of ESRD by 34.16% and 46.17% SBP for 135mmHG and 140mmHg, respectively. The deterministic relative increase in incidence of ESRD (22.3%) associated with a 5mmHg increment in SBP was similar to the MSG (25.8%); using the MTG resulted in a 0% increase in the probability of ESRD. Analysis of the frequency distribution of the MTG displayed areas sparsely populated with random variates. **CONCLUSIONS:** The two PRN generators tested in this analysis produced substantially different results. The differences between the two PRN algorithms were most apparent when predicting relatively rare events, such ESRD. When assessing the internal validity of Monte Carlo simulations the efficieny and robustness of PRN generators should not be assumed.

PRM52

MINIMUM RUN-TIME REQUIREMENTS TO REDUCE MONTE CARLO ERROR IN STOCHASTIC SIMULATIONS

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OBJECTIVES: In health economic modeling the role of probabilistic sensitivity analysis (PSA) is to assess the uncertainty of model predictions with respect to the underlying parameter uncertainty. However, in Monte Carlo simulation parameter uncertainty coincides with and cannot be distinguished from random noise, Monte Carlo error (MCE). The objective of this study was to quantify the minimum run time requirements to reduce MCE to acceptable levels. **METHODS:** An established and validated model, the IMS CORE diabetes model (CDM), was used to compare outcome variability of bootstrap simulations with 1000 repetitions and increasing number of patients ranging from 2500 to 100000. Model projections were defined to evaluate the cost effectiveness of two hypothetical interventions with differences in clinical effectiveness of 0.5% HbA1c and a 2kg weight change in favor of the treatment vs. control arm. Each simulation was performed in three ways; 1st where no parameter sampling was applied, 2nd and 3rd where parameters were sampled around 5% (SE based PSA) and 25% (SD based PSA) of their mean values, respectively. The degree of MCE was determined according to the ratio of the confidence ranges (ICER per QALY) of the non sampling analyses versus PSA. **RESULTS:** The proportion of Monte Carlo error contained in overall ICER variability for simulations with increasing number of patients (2500, 5000, 10000, 25000, 50000 and 100000) was found at 110%, 107%, 73%, 54%, 45% and 32% for SE based PSA and 80%, 80%, 37%, 13%, 9%, and 6% for SD based PSA. **CONCLUSIONS:** Run time requirements to reduce MCE are lower whenever the uncertainty of included parameters is increased. Hypothesizing that not more than 40% of overall outcome variability should be attributable to MCE, the minimum run time requirement was found at 100000 and 10000 patients for SE and SD based PSA, respectively.

PRM53

CAN THE DISUTILITY OF ALLERGIC RHINITIS AND CONJUNCTIVITIS BE CALCULATED FROM THE AGGREGATED TOTAL SYMPTOMS SCORE?

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OBJECTIVES: The use of rhinitis total symptom scores (RTSS) is the recommended method for documenting clinical effect of interventions in allergic rhinitis and conjunctivitis. For cost utility analysis a patient preference measure (health state utility) is needed. We explore whether the disutility of allergic rhinitis can be estimated from RTSS. **METHODS:** We explored the properties of the RTSS and compared these to the properties of the Rhinitis Symptoms Utility Index (RSUI) - a multi-attribute utility function of rhinitis health states. Furthermore, we simulated the outcome of a 2 week period with allergic rhinitis and compared the variation in RSUI associated with each RTSS score to minimal important difference (MID) for utility. **RESULTS:** RTSS is a linear mapping of daily reported rhinitis symptoms with respect to frequency, type, and severity of symptoms. RSUI is multiplicative mapping of frequency, type and severity. This makes the RSUI a non-monotone mapping of RTSS which rules out direct one-to-one mapping from RTSS score to RSUI utility score. The simulation showed that a specific RTSS score can result in very different RSUI values; e.g. a RTSS score of 2.21 (fairly low symptom load) can be associated with a RSUI in the range from 0.376 to 0.784. Since the span of possible RSUI associated with each RTSS score is larger than the MID for utility by any standards, no approximated mapping is not possible without making further assumption on type of symptoms. **CONCLUSIONS:** The RTSS is a standard, recommended measure of clinical effect in rhinitis and conjunctivitis intervention studies; however, further research is needed before patient health state preferences and utility gains from interventions can be estimated from RTSS. These findings emphasize the importance of using validated methods/tools when estimating and comparing utility gains from separate interventions.

PRM54

CORRELATING COST EFFECTIVENESS OUTPUT WITH PATIENT LEVEL DATA INPUT VIA THE IMS CORE DIABETES MODEL (CDM)

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OBJECTIVES: The use of patient level data (PLD) within cost-effectiveness models offers the potential to analyse the relationship between individual input profiles and predicted output. The objective of this study was to ascertain if particular PLD input profiles were predictive of cost effectiveness sub-groups in Type 2 diabetes mellitus (T2DM) subjects. **METHODS:** This study used the IMS Core Diabetes Model (CDM), a validated and established diabetes model to evaluate the cost effectiveness of a new 2ndline oral therapy (Treatment) compared to metformin+ sulphonylurea (Control). Delta treatment effects (favouring Treatment) were a 0.5% HbA1c reduction, 2kg weight change and a difference in symptomatic hypoglycaemia of 0.9/100 patient years. Annual diabetes specific therapy cost was £455 (Treatment) versus £70 (Control). A PLD extract was obtained from NHANES over the period of 1999 to 2008 of T2DM subjects treated with oral therapy only. Costs (2010 UK£) and benefits were discounted at 3.5%. Analysis of input/output data was undertaken using R. **RESULTS:** PLD for 1,858 T2DM subjects from NHANES were obtained with mean age 63.6 years of which 53% were male. Mean estimated cost per QALY of Treatment versus Control was £6,111. Multivariate logistic regression identified age (p<0.05), SBP (p<0.001) and HbA1c (p<0.001) as model input variables significantly associated with cost effectiveness at a willingness to pay (WTP) threshold of £20,000. HbA1c was linearly and negatively correlated with incremental cost (−£569 per 1% increase (p<0.001)). Subjects with baseline HbA1c>7.4% had significantly lower incremental costs compared to those £ 7.4% (£ 1,205 versus £3,462